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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/155,452	10/23/98	BORTS	R 263/PP1R1165

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HM22/0229

EXAMINER

BRUNOVSKIS, F

ART UNIT	PAPER NUMBER
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1632

DATE MAILED:

02/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/155,452

Applicant(s)
Borts et al.

Examiner
Peter Brunovskis

Group Art Unit
1632



☒ Responsive to communication(s) filed on Feb 11, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-10 is/are pending in the application.

Of the above, claim(s) 4, 5, and 8-10 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-3, 6, and 7 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Election/Restriction

Applicant's election of Species b, claims 1-3 and 6-8 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4, 5, 9, and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim 8 is additionally withdrawn from further consideration since it is drawn to nonelected Species a, which is directed to unicellular organisms. Election is considered to be made **without** traverse in Paper No. 10.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter since the claims recite naturally occurring processes. To the extent that the instant claims read on animals, they recite a naturally occurring meiotic

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recombination process in mismatch repair defective animals that can either contain perfectly homologous genetic sequences or up to 30% mismatches. For example, in humans, hereditary non-polyposis colorectal cancer (HNPCC) patients are known to carry defects in mammalian mutS homolog, MSH2 and yet they are reproductively fertile. Meiotic recombination naturally occurs in these patients according to the limitations of claims 1, 2, 6, and 7.

Claim Objections

Claim 3 is objected to because it does clearly relate back its dependent base claim. The process for making the hybrid animal species recited in lines and 2 of claim 3 is a mitotic process. The meiotic recombination process of claim 1 can only occur *following* the making of the hybrid animal species.

Claims 6 and 7 are objected to because of the following informalities: Strictly speaking, recitation of mutS and mutL does not apply to animals which instead carry homologs of mutS and mutL, such as MSH2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-3, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 (and dependent claims) are rendered indefinite by their recitation of the phrase: "to effect meiosis". It is unclear what conditions comprise the limitations of these claims since the conditions do not distinguish between conditions that merely allow meiosis to occur and conditions that actually *effect* (or *cause*) meiosis to occur. Moreover, the metes and bounds of said conditions is unclear.

Claim 2 is rendered indefinite by its recitation of "genes" since the disclosure does not define how broadly the definition of "genes" embraces noncoding sequences such as promoters and 5' and 3' untranslated regions. Moreover there is no connection between a process for meiotic recombination and the mutually exclusive process of forming [en]coded proteins.

Claim 3 is rendered indefinite by its recitation: "by having up to 30% base mismatches with the first DNA sequence and in which an enzymatic mismatch repair system is defective" since it is unclear whether the defective enzymatic mismatch repair system that is being referred to corresponds to the source of the first DNA sequence or the second DNA sequence.

Claim 6 is indefinite since it is unclear *which* eukaryotic cells are being referred to--those comprising the first DNA sequence and/or the second DNA sequence.

Claim 7 is indefinite since it is unclear *which* eukaryotic cells (containing the partially homologous DNA) are being referred to.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining enablement are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation....Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Factors that can be used in evaluating undue experimentation include: the quantity of experimentation necessary, the amount or direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Nature of the invention, guidance and working examples. The specification is almost entirely drawn to a process for making hybrid unicellular organisms, specifically yeast hybrids. The specification makes no reference to making hybrid eukaryotic animals, except perhaps hybrid animal *cells*: "Although the specification envisages the possibility of performing such

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recombinations in bacteria, yeasts, plant or animal cells, in fact the experimental data provided only demonstrate such recombinations in bacteria..." (p. 3, lines 3-6). The specification goes on to say that "[a]lthough the method is applicable in principle to eukaryotes generally, it is expected to be of particular interest in relation to plants and unicellular organisms, such as protozoa, fungi, and particularly yeasts" (sentence abridging pp. 3-4). No further guidance is provided in the specification teaching one of ordinary skill in the art how to employ the methodology in the specification as it applies to unicellular organisms to generate multicellular hybrid animal species.

Claim 3 is confusing since it recites a process for making hybrid animal species (a diploid) according to the meiotic recombination process of claim 1. In the context of animals, meiotic recombination doesn't create any sort of animal, it is involved in the generation of eggs and sperm, for example, that can ultimately enable the production of a "hybrid" species. In the absence of additional method steps, these two processes are mutually exclusive.

Additionally, there is no guidance provided on what type of animal cells to mix, wherein meiotic recombination is to occur in (i.e. spermatogonia, oogonia etc.) or what types of DNA are to constitute the "first" and "second" DNA sequences. Further, it is unclear how mixing such cells together can even lead to the generation of hybrid animal cells since animal cells do not naturally fuse together prior to meiosis. Even if such animal cells were fused (as in yeast), it is unclear whether the process of meiotic recombination described in yeasts could be applied towards making a hybrid multicellular *animal* species. Apart from the inherent unpredictability of making hybrid animals in the absence of any prior attempts or an established methodology, it is

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noted that there is no guidance provided teaching one of ordinary skill in the art how to *use* the hybrid animals of the claimed invention.

Breadth of claims. The claims read on methods for making hybrid animals and are therefore drawn to a broad range of embodiments in which there is nothing known about mismatch repair. The guidance doesn't provide guidance on how to identify cells of those animals which are deficient in mismatch repair. Therefore the disclosure is not enabled for practicing the claimed invention for making hybrid animals wherein the mismatch repair phenotypes have not yet been identified in.

Predictability of the art. The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Amount of experimentation necessary. Given the nature of the invention and the guidance provided, it would likely require considerable experimentation to appropriately develop the claimed method for making hybrid animals.

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For the reasons discussed above, it would require undue experimentation for one skilled in the art to make and use the claimed invention. This is particularly true given the lack of guidance and working examples in the specification, the state of the art, the nature of the invention, the unpredictability of the art, and the amount of experimentation necessary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Thomas (Curr. Opin. Oncol., 6(4):406-412, 1994).

Thomas discloses the relationship between hereditary nonpolyposis colorectal cancer syndromes and a defect in human MSH2, which is homologous to the bacterial mismatch-repair gene MutS (see abstract). Meiotic recombination in patients with this syndrome is an inherent process since these patients are typically capable of producing natural offspring. The meiotic cells are naturally "maintained under conditions to effect meiosis".

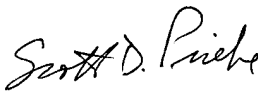
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Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasmine Chambers, can be reached at (703) 308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632


SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER